Remarks/Arguments:

Claims 1-6, 8-12, and 14-16 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicant regards as the invention.

This ground of rejection is based on the examiner's assertion that, because the claims embrace liquid as well as solid dosage forms, some dissociation and/or ionization will take place, such that the claims cannot properly exclude salts or complexes of glucosamine having a counterion having no analgesic activity of its own.

With respect to this ground of rejection, we submit that reliance on dissociation of the claimed compounds is misplaced and has nothing whatsoever to do with the invention. The critical feature of applicants invention is the ratio (now set forth in the claims) at which applicants compositions exhibit synergistic analgesic activity. That is true whether the claimed invention is in solid dosage form or liquid dosage form and whether it is dissociated, undissociated, ionized or unionized.

We believe that what was intended was that the references applied against this application (Giorgetti and Paradies) both contain compositions which are salts or complexes which, if placed in liquid form, would dissociate and produce solutions which allegedly contained the same ratios of material as contemplated by the present invention. For reasons discussed below, applicants submit that neither of those references would ionize or dissociate to produce the synergistic ratios which comprise the present invention. Furthermore, this ground of rejection has now been rendered moot by removal of the exclusionary clause which was the basis for the rejection under 35 U.S.C.112. Withdrawal is respectfully requested.

Claims 1-4 and 6 were rejected under 35 U.S.C. 102 (e) as being anticipated by Giorgetti (B).

The Office Action states that Examples 14 and 31 of Giorgetti "show oral dosage forms comprising glucosamine salts of ketoprofen which meet the limitations of claim 6." This ground for rejection is respectfully traversed for reasons set forth below; and it is presumed that, while the foregoing statement was applied only to claim 6, the examiner intended to indicate that those examples applied to claims 1 - 4 as well as claim 6.

Example 14 of Giorgetti teaches compositions comprising "Ketoprofen glucosamine salt, 1.7 g, equivalent to Ketoprofen acid, 1 g." Based on those numbers, it is

clear that the weight ratio of glucosamine to ketoprofen is 0.7:1. That is also true for the composition of Example 31 except that the ratio is 17g of glucosamine salt which is the equivalent of 10g (i.e., 10% by weight) ketoprofen acid. Thus the ratio is once again 0.7:1, whereas applicants invention, as now claimed requires a glucosamine:analgesic ratio substantially above that taught by Giorgetti. Clearly the ratio taught by Giorgetti is well below that required to produce synergistic pain relief such as that shown in the present application.

For the reasons set forth above, applicants claims clearly distinguish over the teaching of Giorgetti. Accordingly withdrawal of the rejection is respectfully requested.

Claims 1-5, 14, and 15 stand rejected under 35 U.S.C. 103(a) as being unpatentable over Paradies (AH).

Paradies teaches in column 1, lines 20 and following, that the problem addressed "is solved ...by hydrogen-bridge bound complexes having a stoichiometry of 1:1...." between certain alkanoic acids and amino sugars. Among the amino sugars, glucosamine, although not exemplified, is listed at column 2, line 32. This reference, however, only teaches a stoichiometry of 1:1, i.e., that equimolar amounts of the acid and the amino sugar must be utilized. Thus, in example 1 equimolar amounts of ibuprofen and the amino sugar were utilized, and the weight ratio of sugar to analgesic was 0.724:1 (i.e., 181:250). Likewise in example 2, equimolar amounts were used, such that the ratio of amino sugar:ibuprofen was 0.95:1 (i.e., 195.2:206.3).

The Office Action alleges that Claim 2 of Paradies recites a salt of ibuprofen and an amino sugar. That is incorrect in several respects. First, it is clearly disclosed at column 3, lines 1-3, that the disclosed substances "do not involve a salt formation between" ibuprofen and the amino sugar (underlining added for emphasis). Further, Claim 2 incorporates all the limitations of claim 1 and, therefore, only relates to and incorporates the limitation relating to a "complex having a stoichiometry of 1:1, as indicated above. Likewise claim 8 is similarly limited. Paradies does not teach or suggest a weight ratio of about 2:1 or greater or teach or suggest in any that modification of the 1:1 ratio would be required to produce synergistic analgesic activity

In view of the foregoing, applicants claims as currently amended clearly distinguish over the teaching of Paradies. Accordingly withdrawal of this rejection is respectfully requested.

Claims 1-6, 8-12 and 14-16 were rejected under 35 U.S.C. 103(a) as being unpatentable over Petrus (A) in view of either Giorgetti (B) or Paradies (AH).

The Office Action correctly alleged that Petrus teaches a topical ointment formulation comprising 4:1 ratio of glucosamine sulfate to ibuprofen. However, examiner's allegations concerning applicability of Petrus to the present invention, in particular that it motivates one to modify its formula to prepare an oral dosage form, is not understood for reasons which were clearly enunciated in the response to the last office action. Examiner is requested to review those reasons in detail. As specifically set forth in that response, Petrus teaches directly away from an oral dosage form:

> "This topical administration offers a significant advantage over oral administration of therapeutic agents by overcoming the difficult of gastrointestinal absorption...." (Col. 3, lines 36 - 39); and
>
> "The use of a topical, as opposed to an oral or parenteral form of the bio-effective agents, offers four major advantages: they deliver a very high concentration of the bio-effective agents to the desired site; eliminate the possibility of gastrointestinal upset or ulcers; low potential for drug interaction and no skin irritation at the application site." (Col. 11, line 65 - col 12, line 4)

It is hard to imagine how any reference could more clearly teach away from oral administration. Applicants respectfully submit that, in view of this clear teaching, there is no motivation in Petrus to combine this reference with either Giorgetti or Paradies. Further, the required motivation is not provided by either Giorgetti or Paradies, both of which are limited to oral dosage forms which are outside the scope of the present claims and teach away from the ratios needed to achieve the unexpected results shown by the claimed combination.

Applicants respectfully submit that it defies logic to combine two references both of which teach away from the claimed invention and somehow conclude that their combined teaching motivates one skilled in the art to modify each (or either) of them to form the clamed invention. This can only represent a impermissible hindsight attempt to reconstruct applicants invention with applicants disclosure as the only guidance or motivation for the selection of parameters needed to arrive at applicants invention.

For the foregoing reasons, withdrawal of these grounds for rejection is respectfully requested.

Claims 1, 2, 12, 14, and 15, were rejected under 35 U.S.C. 103(a) as being unpatentable over Giorgetti (B).

This ground for rejection is respectfully traversed for the same reasons as those set forth in the above response to the §102(e) rejection based on Giorgetti. Simply stated, there is nothing in Giorgetti which would suggest to one skilled in the art the modification of the ratio of glucosamine to analgesic necessary to produce the unexpected results illustrated by use of the claimed ratios.

In view of the foregoing amendments and remarks, the present invention is believed to distinguish over the art of record and to be in condition for allowance. Accordingly, an early notification to that effect is respectfully requested. In the event that there are still outstanding issues which may be resolved by interview, applicants respectfully request that the examiner contact the undersigned at his convenience by telephone to discuss such issues.

Respectfully submitted,

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